

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

Remarks

Claims 1-42 were pending. Due to the restriction requirement, claims 7, 10-16, 18-35, 37 and 41-42 are cancelled without prejudice to prosecution in a future application. Claim 2 was cancelled and incorporated into claim 1. Claims 43-48 were added. Therefore, claims 1, 3-6, 8-9, 17, 36, and 38-40 and 43 - 48 are now pending.

Applicants thank Examiner Tung for allowing Groups I, II VI, and VII to be examined in the same application.

Summary of Telephone Interview

A telephone interview was conducted with Examiner Tung and Applicants' representative Sheree Lynn Rybak, Ph.D. on May 28, 2004. During this interview, the following claim rejections were discussed. Applicants agreed to amend claims 38-40 so that they refer to SEQ ID NO: 1. However, it was explained to the examiner that SEQ ID NO: 39 is not new matter, as it is clearly shown in FIG. 7.

Applicants also agreed to amend claims 5-6 to include the missing steps, and to amend claims 8-9 and 17 to remove references to the non-elected invention.

The 35 U.S.C. § 102(b) and § 103(a) rejections were discussed. Applicants agreed to introduce the hybridization language of claim 2 into independent claims 1 and 36. The examiner agreed that this would overcome the § 102(b) rejection. To overcome the § 103(a) rejection, Applicants' representative explained to the examiner that although the CCC triplet that would hybridize to the GGG sequence of SEQ ID NO: 1, this CCC sequence would not encode a peptide having tissue repair capabilities (since it only encodes a single amino acid), and further, that even longer sequences that included CCC would not hybridize to SEQ ID NO: 1 under the conditions provided because the similarity between SEQ ID NO: 1 and TGF- β is low. Examiner Tung suggested submitting an alignment of the two sequences, showing the low degree of similarity between SEQ ID NO: 1 and TGF- β . An alignment of the sequence is shown in Exhibit A.

Claim amendments

Claim 1 was amended to include the language of claim 2.

Claim 3 was amended due to the cancellation of claim 2.

Claims 4, 8, 9, and 17 were amended to change the capital “c” in the term “claim” to a lowercase.

Claims 5 and 6 were amended to include the omitted step. Support can be found in claims 5 and 6.

Claims 8, 9, and 17 were amended to remove the peptide language in view of the restriction requirement.

Claim 36 was amended to include the language of claim 2.

Claims 38-40 were amended to change SEQ ID NO: 39 to SEQ ID NO: 1. Support can be found on page 5, lines 19-23.

New Claims

Support for the new claims can be found throughout the specification. For example:

Claim 43: page 4, line 24- page 5, line 6 and SEQ ID NOS: 2 and 3.

Claims 44-45: page 4, lines 12-17 and lines 24-31; page 5, lines 19-28.

Claims 46-47: FIG. 7 and claim 36.

Claim 48: page 4, lines 15-17 and lines 24-26.

Claim objections

Claims 2, 4, 8, 9 and 17 were objected to because the first letter of the term “claim” was capitalized. Applicants have cancelled claim 2 and amended claims 4, 8, 9 and 17 so that the entire term “claim” is in lowercase. Therefore, Applicants request that these claim objections be withdrawn.

35 U.S.C. § 112, first paragraph

Claims 38-40 were rejected under § 112, second paragraph, on the ground that the claims fail to comply with the written description requirement. Applicants have amended these claims so that they refer to SEQ ID NO: 1 instead of SEQ ID NO: 39. Support can be found on page 5, lines 19-23 of the specification. In view of these claim amendments, Applicants request that the 35 U.S.C. § 112, first paragraph rejection be withdrawn.

35 U.S.C. § 112, second paragraph

Claims 5-6 were rejected under 35 U.S.C. § 112, second paragraph, on the ground that the claims omitted an essential step. Applicants have amended these claims to include the omitted step.

Claims 8-9 and 17 were rejected under 35 U.S.C. § 112, second paragraph, on the ground that the claims include both nucleic acid and protein language. In view of the restriction requirement, Applicants amended these claims to remove references to proteins, without prejudice to prosecution in a future application.

In view of these claim amendments, Applicants request that these 35 U.S.C. § 112, second paragraph rejections be withdrawn.

35 U.S.C. § 102(b)

Claims 1, 3-4, 17, and 36 were rejected under 35 U.S.C. § 102(b) as anticipated by Derynck *et al.* (U.S. Patent No. 5,482,851). Applicants disagree and request reconsideration.

Claims 1 and 36 now contain the hybridization language of claim 2. Since Derynck *et al.* do not disclose the hybridization conditions of claims 1 and 36, Derynck *et al.* does not anticipate the claims.

Even without the hybridization language, Derynck *et al.* does not anticipate the claims because claims 1 and 36 are directed to nucleic acid molecules that encode a tissue repair protein. The three nucleotides of TGF- β disclosed in Derynck *et al.* that will hybridize to SEQ ID NO: 1 do not encode a tissue repair protein. In fact, these three nucleotides only encode a single amino acid. Furthermore, the complementary region of SEQ ID NO: 1 is upstream of the open reading frame of SEQ ID NO: 1, and is not found in SEQ ID NO: 39.

Because Derynck *et al.* do not disclose the hybridization conditions specified in claims 1 and 36, and do not disclose a sequence that can hybridize to SEQ ID NO: 1 or 39 which encodes a tissue repair protein, Derynck *et al.* does not anticipate the claims of the present invention. Therefore, Applicants request that the 35 U.S.C. § 102(b) rejection be withdrawn.

35 U.S.C. § 103(a)

Claim 2 was rejected under 35 U.S.C. § 103(a) as obvious in view of Derynck *et al.* Claim 2 has been cancelled, making this rejection moot. However, claim 1 is also not obvious in

view of Derynck *et al.* because the level of stringency provided in the claim is greater than that provided in Derynck *et al.*, and would thus make it even less likely that the TGF- β sequence provided in Derynck *et al.* would hybridize to SEQ ID NO: 1 or 39. As shown in Exhibit A, TGF- β has a low amount of similarity to SEQ ID NO: 1 and 39. Therefore, the higher stringency conditions provided in the claim make it less likely that the sequences disclosed in Derynck *et al.* will hybridize to the nucleic acid molecules claimed.

Similarly, fragments of TGF- β including the CCC sequence will not likely hybridize to SEQ ID NO: 1. For example, shown below is an alignment of 30 nucleotides of porcine TGF- β shown in FIG. 4A of Derynck *et al.* and SEQ ID NO: 1, including the region of hybridization noted in the Office action (underlined). Regions of complementarity where hybridization could occur are shown. Only 11 of the 30 nucleotides could hybridize, indicating a similarity of less than 37%. Those skilled in the art would not expect hybridization between sequences with such low similarity under the stringent condition provided in the claims.

TGF- β (nt 22-51 of GenBank X14150)	catggagaagaa <u>ccc</u> cagagcttcaaggca
nt 44-73 of SEQ ID NO: 1	gcgacctgccggt <u>ggg</u> aactttgtctccga

Claims 8-9 were rejected under 35 U.S.C. § 103(a) as obvious in view of Derynck *et al.* in view of Rolland *et al.* (U.S. Patent 6,184,037). However, for the reasons explained above, Derynck *et al.* does not render the claimed invention obvious.

Because Derynck *et al.*, alone or in combination with other references, do not provide conditions that would permit hybridization between the TGF- β sequence provided in Derynck *et al.* and the claimed nucleic acid molecules, the claimed invention is not obvious. Therefore, Applicants request that the 35 U.S.C. § 103(a) rejections be withdrawn.

Sequence Rules

SEQ ID NO: 39 is a nucleic acid sequence showing the open reading frame of SEQ ID NO: 1. The sequence listing filed on August 1, 2001 did not include SEQ ID NO: 39. The sequence listing filed on October 1, 2001 included SEQ ID NO: 39. Please use the sequence listing filed on October 1, 2001 that includes SEQ ID NO: 39.

Although SEQ ID NO: 39 was not provided in the sequence listing originally filed, the sequence provided in SEQ ID NO: 39 was provided in FIG. 7 as published in the PCT application. Therefore, SEQ ID NO: 39 is not new matter. Applicants request that the sequence listing showing SEQ ID NO: 39 be used, as it does not include new matter.

Priority


United Kingdom application 9900167.9 filed January 6, 1999 does not have FIG. 7, which specifically discloses FIG. 7. Therefore, the priority date for SEQ ID NO: 39 is January 6, 2000.

If any matters remain before a notice of allowance is issued, the examiner is invited to telephone the undersigned.

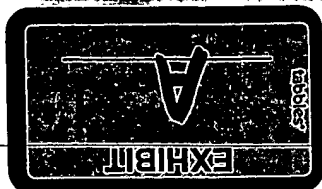
Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By


Sheree Lynn Rybak, Ph.D.
Registration No. 47,913

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 226-7391
Facsimile: (503) 228-9446



1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100																																																																																																					
1000	990	980	970	960	950	940	930	920	910	900	890	880	870	860	850	840	830	820	810	800	790	780	770	760	750	740	730	720	710	700	690	680	670	660	650	640	630	620	610	600	590	580	570	560	550	540	530	520	510	500	490	480	470	460	450	440	430	420	410	400	390	380	370	360	350	340	330	320	310	300	290	280	270	260	250	240	230	220	210	200	190	180	170	160	150	140	130	120	110	100	90	80	70	60	50	40	30	20	10	0	-10	-20	-30	-40	-50	-60	-70	-80	-90	-100	-110	-120	-130	-140	-150	-160	-170	-180	-190	-200	-210	-220	-230	-240	-250	-260	-270	-280	-290	-300	-310	-320	-330	-340	-350	-360	-370	-380	-390	-400	-410	-420	-430	-440	-450	-460	-470	-480	-490	-500	-510	-520	-530	-540	-550	-560	-570	-580	-590	-600	-610	-620	-630	-640	-650	-660	-670	-680	-690	-700	-710	-720	-730	-740	-750	-760	-770	-780	-790	-800	-810	-820	-830	-840	-850	-860	-870	-880	-890	-900	-910	-920	-930	-940	-950	-960	-970	-980	-990	-1000